

reacting the nucleoside with tosyl chloride in pyridine at room temperature for about 24 hours, working up the product in the usual manner (e.g., by washing, drying, and crystallizing it).

The triphosphate can be prepared according to the procedure of Hoard et al., *J. Am. Chem. Soc.*, 87(8), 1785–1788 (1965). For FTC is activated (by making a imidazolidine, according to methods known to those skilled in the art) and treating with tributyl ammonium pyrophosphate in DMF. The reaction gives primarily the triphosphate of the nucleoside, with some unreacted monophosphate and some diphosphate. Purification by anion exchange chromatography of a DEAE column is followed by isolation of the triphosphate, e.g., as the tetrasodium salt.

This invention has been described with reference to its preferred embodiments. Variations and modifications of the invention, a method of resolution and antiviral activity of nucleoside enantiomers, will be obvious to those skilled in the art from the foregoing detailed description of the invention. It is intended that all of these variations and modifications be included within the scope of the appended claims.

We claim:

1. The (–)-enantiomer of cis-4-amino-5-fluoro-1-(2-hydroxymethyl-1,3-oxathiolane-5-yl)-(1H)-pyrimidin-2-one that is at least 95% free of the corresponding (+)-enantiomer.

2. (–)-Cis-4-amino-5-fluoro-1-(2-hydroxymethyl-1,3-oxathiolane-5-yl)-(1H)-pyrimidin-2-one or a pharmaceutically acceptable salt, ester or salt of an ester thereof.

3. The substantially pure (–)-enantiomer of cis-4-amino-5-fluoro-1-(2-hydroxymethyl-1,3-oxathiolane-5-yl)-(1H)-pyrimidin-2-one or a pharmaceutically acceptable salt, ester, or salt of an ester thereof, wherein the (+) enantiomer is present in an amount of no more than 5% w/w.

4. The compound of claim 3 wherein the (+)-enantiomer is present in an amount of no more than about 2% w/w.

5. The compound of claim 3 wherein the (+)-enantiomer is present in an amount of less than 1% w/w.

6. A pharmaceutical composition comprising a compound as claimed in any one of claims 2–5 in combination with a pharmaceutically acceptable carrier.

7. (–)-Cis-4-amino-5-fluoro-1-(2-hydroxymethyl-1,3-oxathiolane-5-yl)-(1H)-pyrimidin-2-one or a pharmaceutically acceptable salt thereof.

8. The 5'-O-alkyl derivative of the (–)-enantiomer of cis-4-amino-5-fluoro-1-(2-hydroxymethyl-1,3-oxathiolane-5-yl)-(1H)-pyrimidin-2-one.

9. The 5'-O-alkylC(O)-derivative of the (–)-enantiomer of cis-4-amino-5-fluoro-1-(2-hydroxymethyl-1,3-oxathiolane-5-yl)-(1H)-pyrimidin-2-one.

10. The derivative of claim 9, wherein alkylC(O)— is selected from the group consisting of acetic, propionic, butyric, and pentanoic.

11. The monophosphate, diphosphate, or triphosphate of the (–)-enantiomer of cis-4-amino-5-fluoro-1-(2-hydroxymethyl-1,3-oxathiolane-5-yl)-(1H)-pyrimidin-2-one.

12. A pharmaceutically acceptable salt of the (–)-enantiomer of cis-4-amino-5-fluoro-1-(2-hydroxymethyl-1,3-oxathiolane-5-yl)-(1H)-pyrimidin-2-one that is at least 95% free of the corresponding (+)-enantiomer.

13. A pharmaceutical composition comprising an effective HIV treatment amount for humans of the (–)-enantiomer of cis-4-amino-5-fluoro-1-(2-hydroxymethyl-1,3-oxathiolane-5-yl)-(1H)-pyrimidin-2-one that is at least 95% free of the corresponding (+)-enantiomer, in combination with a pharmaceutically acceptable carrier or diluent.

14. A pharmaceutical composition comprising an effective HIV treatment amount for humans of the (–)-enantiomer of a pharmaceutically acceptable salt of a compound of cis-4-amino-5-fluoro-1-(2-hydroxymethyl-1,3-oxathiolane-5-yl)-(1H)-pyrimidin-2-one that is at least 95% free of the corresponding (+)-enantiomer, in combination with a pharmaceutically acceptable carrier or diluent.

15. The pharmaceutical composition of claim 13, in a form for oral administration.

16. The pharmaceutical composition of claim 15, wherein the composition is in tablet form.

17. The pharmaceutical composition of claim 15, wherein the composition is in capsule form.

18. The pharmaceutical composition of claim 13, wherein the composition is a liquid.

19. The pharmaceutical composition of claim 13, in a form for intravenous administration.

20. The pharmaceutical composition of claim 19, wherein the carrier comprises a sterile diluent for injection.

21. The pharmaceutical composition of claim 13, in a form for topical administration.

22. The pharmaceutical composition of claim 14, in a form for oral administration.

23. The pharmaceutical composition of claim 22, wherein the composition is in tablet form.

24. The pharmaceutical composition of claim 22, wherein the composition is in capsule form.

25. The pharmaceutical composition of claim 14, wherein the composition is a liquid.

26. The pharmaceutical composition of claim 14, in a form for intravenous administration.

27. The pharmaceutical composition of claim 17, wherein the carrier comprises a sterile diluent for injection.

28. The pharmaceutical composition of claim 14, in a form for topical administration.

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